NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF 1-CHLORO-2-PROPANOL
(TECHNICAL GRADE)

(CAS NO. 127-00-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

September 1998

NTP TR 477

NIH Publication No. 98-3967

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. The prechronic and chronic studies were conducted in compliance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, and all aspects of the chronic studies were subjected to retrospective quality assurance audits before being presented for public review.

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology and carcinogenesis studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Technical Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

Listings of all published NTP reports and ongoing studies are available from NTP Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709 (919-541-3419). The Abstracts and other study information for 2-year studies are also available at the NTP's World Wide Web site: http://ntp-server.niehs.nih.gov.

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF 1-CHLORO-2-PROPANOL
(TECHNICAL GRADE)

(CAS NO. 127-00-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

September 1998

NTP TR 477

NIH Publication No. 98-3967

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

CONTRIBUTORS

National Toxicology Program
Evaluated and interpreted results and reported findings

J.K. Dunnick, Ph.D., Study Scientist
D.A. Bridge, B.S.
J.R. Bucher, Ph.D.
R.E. Chapin, Ph.D.
J.R. Hailey, D.V.M.
J.K. Haseman, Ph.D.
R.R. Maronpot, D.V.M.
G.N. Rao, D.V.M., Ph.D.
C.S. Smith, Ph.D.
G.S. Travlos, D.V.M.
D.B. Walters, Ph.D.
K.L. Witt, M.S., Integrated Laboratory Systems

SRI International
Conducted 14-day and 14-week studies, evaluated pathology findings

J.B. Reid, Ph.D., Principal Investigator
R.A. Becker, Ph.D.
J.R. Hill, Ph.D.
E.F. Meierhenry, Ph.D.

TSI Mason Laboratories
Conducted 2-year studies, evaluated pathology findings

M.R. Osheroff, Ph.D., Principal Investigator
C. Gamba-Vitalo, Ph.D.
F.A. Voelker, D.V.M.
D. Norlin, Ph.D.

Experimental Pathology Laboratories, Inc.
Provided pathology quality assurance

J.F. Hardisty, D.V.M., Principal Investigator
J. Peckham, D.V.M., M.S., Ph.D.

Dynamac Corporation
Prepared quality assurance audits

S. Brecher, Ph.D., Principal Investigator

NTP Pathology Working Group
Evaluated slides, prepared pathology report on rats (24 April 1997)

J.C. Seely, D.V.M., Chairperson
PATHCO, Inc.
R. Brown, D.V.M.
Glaxo-Wellcome
V. Geiss, D.V.M., Ph.D., Observer
National Toxicology Program
J.R. Hailey, D.V.M.
National Toxicology Program
R.A. Herbert, D.V.M., Ph.D.
National Toxicology Program
J.R. Leininger, D.V.M., Ph.D.
National Toxicology Program
J. Peckham, D.V.M., M.S., Ph.D.
Experimental Pathology Laboratories, Inc.
A. Radovsky, D.V.M., Ph.D.
National Toxicology Program

Evaluated slides, prepared pathology report on mice (24 April 1997)

P.K. Hildebrandt, D.V.M., Chairperson
PATHCO, Inc.
R. Brown, D.V.M.
Glaxo-Wellcome
V. Geiss, D.V.M., Ph.D., Observer
National Toxicology Program
J.R. Hailey, D.V.M.
National Toxicology Program
R.A. Herbert, D.V.M., Ph.D.
National Toxicology Program
J.R. Leininger, D.V.M., Ph.D.
National Toxicology Program
J. Peckham, D.V.M., M.S., Ph.D.
Experimental Pathology Laboratories, Inc.
A. Radovsky, D.V.M., Ph.D.
National Toxicology Program

Analytical Sciences, Inc.
Provided statistical analyses

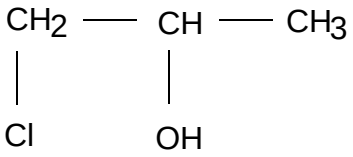
R.W. Morris, M.S., Principal Investigator
S.R. Lloyd, M.S.
N.G. Mintz, B.S.

Biotechnical Services, Inc.
Prepared Technical Report

S.R. Gunnels, M.A., Principal Investigator
G. Gordon, M.A.
L.M. Harper, B.S.
A.M. Macri-Hanson, M.A., M.F.A.
S.M. Swift, B.S.

CONTENTS

ABSTRACT



TECHNICAL GRADE 1-CHLORO-2-PROPANOL

(~ 75% 1-CHLORO-2-PROPANOL; ~ 25% 2-CHLORO-1-PROPANOL)

CAS No. 127-00-4

Chemical Formula: C_3H_7ClO Molecular Weight: 94.54

Synonyms: Chlorohydrin, 1-chloro-2-hydroxypropane, 1-chloroisopropyl alcohol, propylene-∝-chlorohydrin, *sec*-propylene chlorohydrin

1-Chloro-2-propanol and its positional isomer, 2-chloro-1-propanol, are used as chemical intermediates for the manufacture of propylene oxide, a starting material for production of polyurethane polyols and propylene glycol. The National Cancer Institute nominated 1-chloro-2-propanol for study because of potential for human exposure due to its residues in various foods that are fumigated with ethylene oxide or propylene oxide. Male and female F344/N rats and $B6C3F_1$ mice were exposed to technical grade 1-chloro-2-propanol (75% to 76% 1-chloro-2-propanol; 24% to 25% 2-chloro-1-propanol) in drinking water for 14 days, 14 weeks, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, *Drosophila melanogaster*, and mouse peripheral blood erythrocytes. Continuous breeding studies were conducted in Sprague-Dawley rats.

14-DAY STUDY IN RATS

Groups of 10 male and 10 female F344/N rats were administered 1-chloro-2-propanol in drinking water at concentrations of 0, 100, 330, 1,000, 3,300, or 10,000 ppm for 14 days. Two 10,000 ppm females died before the end of the study. The final mean body weights and body weight gains of 3,300 and 10,000 ppm rats were significantly less than those of the controls; rats in the 10,000 ppm groups lost weight. Water consumption by the 3,300 and 10,000 ppm groups was significantly less than that by the controls throughout the study. The thymus weights of 10,000 ppm rats were significantly less than those of the controls. Exposure to 1-chloro-2-propanol caused cytoplasmic alteration and degeneration of the acinar cells and fatty change in the pancreas, atrophy of the bone marrow, and atrophy and hematopoiesis of the spleen in males and females.

14-DAY STUDY IN MICE

Groups of 10 male and 10 female $B6C3F_1$ mice were administered 1-chloro-2-propanol in drinking water at concentrations of 0, 100, 330, 1,000, 3,300, or 10,000 ppm for 14 days. One male mouse in the 10,000 ppm group died before the end of the study. Mean body weight gains of 10,000 ppm mice were significantly less than those of the controls. Water consumption by 3,300 and 10,000 ppm males and females was significantly less than that by the controls throughout the study. Liver weights of 1,000, 3,300, or 10,000 ppm males and females were significantly greater and thymus weights of 10,000 ppm mice were significantly less than those of the controls. Exposure

to 1-chloro-2-propanol caused hepatocellular vacuolization, cytoplasmic alteration and degeneration of the pancreas acinar cells, and atrophy of the spleen in males and females.

14-WEEK STUDY IN RATS

Groups of 10 male and 10 female F344/N rats were administered 1-chloro-2-propanol at concentrations of 0, 33, 100, 330, 1,000, or 3,300 ppm (equivalent to average daily doses of approximately 5, 10, 35, 100, or 220 mg/kg) for 14 weeks. All rats survived to the end of the study. Mean body weight gains of 3,300 ppm rats were significantly less than those of the controls. Water consumption by the 3,300 ppm male and female rats was significantly less than that by the controls. A minimal to mild anemia was observed in exposed female rats. The cauda epididymis and epididymis weights of 3,300 ppm males were significantly less than those of the controls. The percentage of abnormal sperm in 3,300 ppm males and the concentration of epididymal sperm in 330 ppm males were significantly increased compared to the controls. Kidney and liver weights of males and females exposed to 100 ppm or more were generally greater than those of the controls. The incidences of acinar cell degeneration and fatty change of the pancreas in 1,000 and 3,300 ppm rats, hepatocytic metaplasia of the pancreatic islets in 3,300 ppm females, cytoplasmic vacuolization of the liver in 100, 1,000 and 3,300 ppm males, and renal tubule epithelium regeneration in 3,300 ppm females were increased compared to the controls.

14-WEEK STUDY IN MICE

Groups of 10 male and 10 female B6C3F$_1$ mice were administered 1-chloro-2-propanol in drinking water at concentrations of 0, 33, 100, 330, 1,000, or 3,300 ppm (equivalent to average daily doses of approximately 5, 15, 50, 170, or 340 mg/kg to males and 7, 20, 70, 260, or 420 mg/kg to females) for 14 weeks. One 330 ppm male died before the end of the study. Mean body weight gains of exposed groups were similar to those of the controls. A minimal anemia was observed in 3,300 ppm males. The right epididymis weight of 3,300 ppm males was significantly greater than that of the controls. Kidney weights of 3,300 ppm mice, liver weights of 1,000 ppm males and of all exposed groups of females, and thymus weights of 1,000 and 3,300 ppm females were greater than those of the controls. The incidences of pancreatic acinar cell degeneration and fatty change in 3,300 ppm males and females and cytoplasmic vacuolization of the liver in all groups of exposed females were significantly increased compared to the controls. The severities of renal tubule cytoplasmic vacuolization were greater in 1,000 and 3,300 ppm males than in the controls.

2-YEAR STUDY IN RATS

Groups of 50 male and 50 female F344/N rats were administered drinking water containing 0, 150, 325, or 650 ppm 1-chloro-2-propanol (equivalent to average daily doses of approximately 15, 30, or 65 mg/kg during the first several months of the study and 8, 17, or 34 mg/kg for the remainder of the 2-year study) for up to 105 weeks. Survival of all exposed groups was similar to that of the controls. Mean body weights of exposed rats were generally similar to those of the controls throughout most of the study. Water consumption by all exposed groups was similar to that by the controls. No treatment-related neoplasms or nonneoplastic lesions were observed in this study.

2-YEAR STUDY IN MICE

Groups of 50 male and 50 female B6C3F$_1$ mice were administered drinking water containing 0, 250, 500, or 1,000 ppm 1-chloro-2-propanol (equivalent to average daily doses of approximately 45, 75, or 150 mg/kg to males and 60, 105, or 210 mg/kg to females during the first several months of the study and 25, 50, or 100 mg/kg for the remainder of the 2-year study) for up to 105 weeks. Survival of all exposed groups was similar to that of the controls. The mean body weights of all exposed mice were generally similar to those of the controls throughout the study. Water consumption by all exposed groups was similar to that by the controls. No treatment-related neoplasms or nonneoplastic lesions were observed in this study.

GENETIC TOXICOLOGY

1-Chloro-2-propanol is a demonstrated mutagen *in vitro*. It was weakly mutagenic in *S. typhimurium* strain TA100 in the presence of hamster or rat liver S9 activation enzymes and was positive, with and without S9, in TA1535. No mutagenic activity was detected in strains TA97, TA98, and TA1537, with or without S9. In cytogenetic tests with Chinese hamster ovary cells, 1-chloro-2-propanol induced high levels of sister

chromatid exchanges and chromosomal aberrations in the presence and the absence of S9. The marked ability of 1-chloro-2-propanol to induce chromosomal effects *in vitro* was not seen *in vivo*. Positive results were obtained in a test in *D. melanogaster* for induction of sex-linked recessive lethal mutations in germ cells of males administered 1-chloro-2-propanol via injection; however, negative results were obtained when males were administered 1-chloro-2-propanol in feed. A subsequent germ cell reciprocal translocation test in *D. melanogaster* yielded negative results. Further, no induction of micronucleated erythrocytes was observed in peripheral blood of male and female mice administered 1-chloro-2-propanol via drinking water for 14 weeks.

CONCLUSIONS

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity** of technical grade 1-chloro-2-propanol in male or female F344/N rats exposed to 150, 325, or 650 ppm. There was *no evidence of carcinogenic activity* of technical grade 1-chloro-2-propanol in male or female B6C3F_1 mice exposed to 250, 500, or 1,000 ppm.

---

* Explanation of Levels of Evidence of Carcinogenic Activity is on page 9. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 11.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of 1-Chloro-2-propanol

	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Concentrations	0, 150, 325, or 650 ppm	0, 150, 325, or 650 ppm	0, 250, 500, or 1,000 ppm	0, 250, 500, or 1,000 ppm
Body weights	Exposed groups similar to control group	Exposed groups similar to control group	Exposed groups similar to control group	Exposed groups similar to control group
Survival rates	20/50, 23/50, 24/50, 23/50	25/50, 33/50, 30/50, 31/50	40/50, 44/50, 29/50, 39/50	32/50, 32/50, 36/50, 32/50
Nonneoplastic effects	None	None	None	None
Neoplastic effects	None	None	None	None
Level of evidence of carcinogenic activity	No evidence	No evidence	No evidence	No evidence
Genetic toxicology				
Salmonella typhimurium gene mutations:	Positive or equivocal with S9 in strain TA100; positive with and without S9 in strain TA1535; negative with and without S9 in strains TA97, TA98, and TA1537			
Sister chromatid exchanges				
Cultured Chinese hamster ovary cells *in vitro*:	Positive with and without S9			
Chromosomal aberrations				
Cultured Chinese hamster ovary cells *in vitro*:	Positive with and without S9			
Sex-linked recessive lethal mutations				
Drosophila melanogaster:	Positive when administered via injection, negative when administered via feed			
Reciprocal translocations				
Drosophila melanogaster:	Negative			
Micronucleated erythrocytes				
Mouse peripheral blood *in vivo*:	Negative			

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

The National Toxicology Program describes the results of individual experiments on a chemical agent and notes the strength of the evidence for conclusions regarding each study. Negative results, in which the study animals do not have a greater incidence of neoplasia than control animals, do not necessarily mean that a chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a chemical is carcinogenic for laboratory animals under the conditions of the study and indicate that exposure to the chemical has the potential for hazard to humans. Other organizations, such as the International Agency for Research on Cancer, assign a strength of evidence for conclusions based on an examination of all available evidence, including animal studies such as those conducted by the NTP, epidemiologic studies, and estimates of exposure. Thus, the actual determination of risk to humans from chemicals found to be carcinogenic in laboratory animals requires a wider analysis that extends beyond the purview of these studies.

Five categories of evidence of carcinogenic activity are used in the Technical Report series to summarize the strength of the evidence observed in each experiment: two categories for positive results (**clear evidence** and **some evidence**); one category for uncertain findings (**equivocal evidence**); one category for no observable effects (**no evidence**); and one category for experiments that cannot be evaluated because of major flaws (**inadequate study**). These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Report series to incorporate more specifically the concept of actual weight of evidence of carcinogenic activity. For each separate experiment (male rats, female rats, male mice, female mice), one of the following five categories is selected to describe the findings. These categories refer to the strength of the experimental evidence and not to potency or mechanism.

- **Clear evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- **Some evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
- **Equivocal evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemical related.
- **No evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- **Inadequate study** of carcinogenic activity is demonstrated by studies that, because of major qualitative or quantitative limitations, cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

When a conclusion statement for a particular experiment is selected, consideration must be given to key factors that would extend the actual boundary of an individual category of evidence. Such consideration should allow for incorporation of scientific experience and current understanding of long-term carcinogenesis studies in laboratory animals, especially for those evaluations that may be on the borderline between two adjacent levels. These considerations should include:

- adequacy of the experimental design and conduct;
- occurrence of common versus uncommon neoplasia;
- progression (or lack thereof) from benign to malignant neoplasia as well as from preneoplastic to neoplastic lesions;
- some benign neoplasms have the capacity to regress but others (of the same morphologic type) progress. At present, it is impossible to identify the difference. Therefore, where progression is known to be a possibility, the most prudent course is to assume that benign neoplasms of those types have the potential to become malignant;
- combining benign and malignant tumor incidence known or thought to represent stages of progression in the same organ or tissue;
- latency in tumor induction;
- multiplicity in site-specific neoplasia;
- metastases;
- supporting information from proliferative lesions (hyperplasia) in the same site of neoplasia or in other experiments (same lesion in another sex or species);
- presence or absence of dose relationships;
- statistical significance of the observed tumor increase;
- concurrent control tumor incidence as well as the historical control rate and variability for a specific neoplasm;
- survival-adjusted analyses and false positive or false negative concerns;
- structure-activity correlations; and
- in some cases, genetic toxicology.

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on 1-chloro-2-propanol on 10 December 1997 are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing the NTP studies:

- to ascertain that all relevant literature data have been adequately cited and interpreted,
- to determine if the design and conditions of the NTP studies were appropriate,
- to ensure that the Technical Report presents the experimental results and conclusions fully and clearly,
- to judge the significance of the experimental results by scientific criteria, and
- to assess the evaluation of the evidence of carcinogenic activity and other observed toxic responses.

Gary P. Carlson, Ph.D., Chairperson
School of Health Sciences
Purdue University
West Lafayette, IN

A. John Bailer, Ph.D.
Department of Mathematics and Statistics
Miami University
Oxford, OH

Steven A. Belinsky, Ph.D.*
Inhalation Toxicology Research Institute
Kirkland Air Force Base
Albuquerque, NM

James S. Bus, Ph.D., Principal Reviewer
Health and Environmental Sciences
Dow Chemical Company
Midland, MI

Linda A. Chatman, D.V.M., Principal Reviewer
Pfizer, Inc.
Groton, CT

John M. Cullen, Ph.D., V.M.D.
Department of Microbiology, Parasitology, and Pathology
College of Veterinary Medicine
North Carolina State University
Raleigh, NC

Susan M. Fischer, Ph.D.
M.D. Anderson Cancer Center
University of Texas
Smithville, TX

Thomas L. Goldsworthy, Ph.D.
Integrated Laboratory Systems
Research Triangle Park, NC

Irma Russo, M.D.
Fox Chase Cancer Center
Philadelphia, PA

Special Reviewers

Stephen S. Hecht, Ph.D.
University of Minnesota Cancer Centers
Minneapolis, MN

Michele Medinsky, Ph.D.
Chemical Industry Institute of Toxicology
Research Triangle Park, NC

Jose Russo, M.D., Principal Reviewer
Fox Chase Cancer Center
Philadelphia, PA

---

* Did not attend

SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On 10 December 1997, the draft Technical Report on the toxicology and carcinogenesis studies of 1-chloro-2-propanol (technical grade) received public review by the National Toxicology Program's Board of Scientific Counselors' Technical Reports Review Subcommittee. The meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. J.K. Dunnick, NIEHS, introduced the toxicology and carcinogenesis studies of 1-chloro-2-propanol by discussing the uses of the chemical and the rationale for study, describing the experimental design, reporting on any survival and body weight effects, and commenting on compound-related neoplastic and nonneoplastic lesions in rats and mice. The proposed conclusions for the 2-year studies were *no evidence of carcinogenic activity* in male or female F344/N rats or $B6C3F_1$ mice.

Dr. Chatman, a principal reviewer, agreed with the proposed conclusions. She noted that the pancreas was a target tissue in the 14-week studies, and in light of epidemiologic reports of higher rates of pancreatic cancer in humans working in the chlorohydrin industry, she asked if the top doses should have been higher in the 2-year studies. Dr. Chatman asked why inhalation was not the preferred route of exposure. Dr. Dunnick responded that the chemical was administered orally because of concern about its being present in fumigated foods.

Dr. J. Russo, the second principal reviewer, agreed with the proposed conclusions. He commented on the significant decrease in drinking water consumption in exposed animals in the 14-week studies and asked whether this could be due to some type of hypothalamic damage. Dr. Dunnick said water consumption was decreased more in the 14-day studies than in the 14-week studies, and by 13 weeks, decreases in water consumption were much less as animals adapted to the taste of the chemical. Dr. Chatman inquired whether exposure concentrations were monitored in view of the decrease in water consumption. Dr. Dunnick said analyses were performed on the drinking water bottles and on the dose preparations, and, in general, concentrations were within targeted amounts.

Dr. Bus, the third principal reviewer, agreed with the proposed conclusions.

Dr. Goldsworthy also thought that the high doses may have been below maximal tolerated doses. Dr. J.R. Hailey, NIEHS, said that the 2-year study doses were based on the significant pancreatic lesions in the 14-week studies. Dr. Bus commented that based on the results of the 14-week studies, the doses for the 2-year studies were chosen properly. Dr. Cullen asked whether the pancreatic lesions in the 14-week studies were metaplastic and if the size of the pancreas had changed. Dr. Hailey replied that there was no change in size although there was apoptosis of acinar cells and replacement by adipocytes (fat cells). Dr. Chatman urged the NTP to pursue the evaluation of possible pancreatic effects in view of a possible association with increased pancreatic cancer in the workplace.

Dr. Chatman moved that the Technical Report on 1-chloro-2-propanol (technical grade) be accepted with the conclusions as written for male and female rats and mice, *no evidence of carcinogenic activity*. Dr. Goldsworthy seconded the motion, which was accepted unanimously with seven votes.